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APPLICATION NO. FILING DATE		FIRST NAMED INVENTOR		ATTORNEY D	ATTORNEY DOCKET NO.		
09/889,982	-	01/14/2002		Tariq M Rana	1368-17	PCT/US	4387
23869	7590	11/17/2004			EXAMINER		
	ARON, LLP	PARKIN, JEFFREY S					
	6900 JERICHO TURNPIKE SYOSSET, NY 11791				ART U	NIT	PAPER NUMBER
,					164	1648	
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Please find below and/or attached an Office communication concerning this application or proceeding.

,	Application No.	Applicant(s)
	09/889,982	RANA ET AL.
Office Action Summary	Examiner	Art Unit
	Jeffrey S. Parkin, Ph.D.	1648
The MAILING DATE of this communication apperent of the second for Reply	ears on the cover sheet with the c	orrespondence address
A SHORTENED STATUTORY PERIOD FOR REPLY THE MAILING DATE OF THIS COMMUNICATION.  - Extensions of time may be available under the provisions of 37 CFR 1.13 after SIX (6) MONTHS from the mailing date of this communication.  - If the period for reply specified above is less than thirty (30) days, a reply If NO period for reply is specified above, the maximum statutory period w.  - Failure to reply within the set or extended period for reply will, by statute, Any reply received by the Office later than three months after the mailing earned patent term adjustment. See 37 CFR 1.704(b).	6(a). In no event, however, may a reply be tim within the statutory minimum of thirty (30) days ill apply and will expire SIX (6) MONTHS from cause the application to become ABANDONET	rely filed s will be considered timely. the mailing date of this communication. D (35 U.S.C. § 133).
Status		
1) Responsive to communication(s) filed on 20 Fe	bruary 2004.	
	action is non-final.	
Since this application is in condition for allowan closed in accordance with the practice under Expression in the practice of the condition of the conditi		
Disposition of Claims		
4) ☐ Claim(s) 1-5,7-9,16-19,27 and 28 is/are pending 4a) Of the above claim(s) is/are withdraw 5) ☐ Claim(s) is/are allowed.  6) ☐ Claim(s) 1-5,7-9,16-19,27 and 28 is/are rejected 7) ☐ Claim(s) is/are objected to.  8) ☐ Claim(s) are subject to restriction and/or	n from consideration.	
Application Papers		
9)☐ The specification is objected to by the Examiner		
10) ☐ The drawing(s) filed on is/are: a) ☐ acce	pted or b) $\square$ objected to by the E	xaminer.
Applicant may not request that any objection to the d	-	, ,
Replacement drawing sheet(s) including the correction 11) The oath or declaration is objected to by the Example 11.		
Priority under 35 U.S.C. § 119		
a) ☐ Acknowledgment is made of a claim for foreign part a) ☐ All b) ☐ Some * c) ☐ None of:  1. ☐ Certified copies of the priority documents 2. ☐ Certified copies of the priority documents 3. ☐ Copies of the certified copies of the priorical application from the International Bureau * See the attached detailed Office action for a list of	have been received. have been received in Application by documents have been receive (PCT Rule 17.2(a)).	on No d in this National Stage
Attachment(s)		
Notice of References Cited (PTO-892)	4) Interview Summary (	
2) Notice of Draftsperson's Patent Drawing Review (PTO-948) B) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date	Paper No(s)/Mail Dat 5) Notice of Informal Pa 6) Other:	

Serial No.: 09/889,982 Docket No.: 13257-00018
Applicants: Rana, T. M., et al. Filing Date: 01/14/02

# Response to Amendment

#### Status of the Claims

Acknowledgement is hereby made of receipt and entry of the amendment filed 20 February, 2004, wherein claims 6, 10-15, and 20-26 were canceled without prejudice or disclaimer, claim 16 amended, and new claims 27 and 28 introduced. Claims 1-5, 7-9, 16-19, 27, and 28 are pending in the instant application.

# 35 U.S.C. § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

### Written Description

Claims 1-5, 7-9, 16-19, 27, and 28 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In re Rasmussen, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). In re Wertheim, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). In re Rochester, 358 F.3d 916, 69 U.S.P.Q.2d 1886 (C.A.F.C. 2004). The claims are broadly directed toward an "oligourea" comprising a basic-arginine rich region of Tat. No further structural limitations are provided in the claim language.

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the

inventor had possession of the claimed invention. See, e.g., Vas-Cath, Inc., v. Mahurkar, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. The issue raised in this application is whether the original application provides adequate support for the broadly claimed genus of oligourea derivatives. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or artrecognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the biomolecule of interest. In re Bell, 991 F.2d 781, 26 U.S.P.Q.2d 1529 (Fed. Cir. 1993). In re Deuel, 51 F.3d 1552, 34 U.S.P.O.2d 1210 (Fed. Cir. 1995). A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., Fujikawa v. Wattanasin, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1995). The court noted in this decision that a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not reasonably lead those skilled in the art to any particular species.

An applicant may show possession of an invention by disclosure of drawings or structural chemical formulas that are sufficiently

detailed to show that applicant was in possession of the claimed invention as a whole. An applicant may also show that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics. biomolecules, examples For some identifying characteristics include a nucleotide or amino acid structure, binding affinity, sequence, chemical The written description specificity, and molecular weight. requirement may be satisfied through disclosure of function and minimal structure when there is a well-established correlation between structure and function. Without such a correlation, the capability to recognize or understand the structure form the mere recitation of function and minimal structure is highly unlikely. In the latter case, disclosure of function alone is little more than a wish for possession; it does not satisfy the written description requirement. Regents of the University of California v. Eli Lilly, 119 F.3d 1559, 1566, 43 U.S.P.Q.2d 1398, 1404, 1406 (Fed. Cir. 1997), cert. denied, 523 U.S. 1089 (1998). In re Wilder, 736 F.2d 1516, 1521, 222 U.S.P.Q. 369, 372-3 (Fed. Cir. 1984). Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention.

The claims of the instant application are broadly directed toward any oligourea simply comprising the basic-arginine rich region of Tat. The disclosure appears to describe a specific compound having the following structural formula set forth in

Figure 1B wherein  $R_1$  and  $R_2$  comprising the arginine-rich region of HIV-1 set forth in Figure 1A. However, the claims fail to provide any significant structural limitations. They simply stipulate that the composition comprises an oligourea. The disclosure fails to provide any guidance pertaining to acceptable side-chain substitutions ( $R_1/R_2$ ) or the length of the oligourea. Accordingly, the skilled artisan cannot readily envisage any additional molecules.

## Enablement

Claims 1-5, 7-9, 16-19, 27, and 28 are rejected under 35 U.S.C. § 112, first paragraph, because the specification does not reasonably enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The disclosure appears to describe the preparation of a single compound comprising the oligourea set forth in Figure 1B wherein the side-chain substituents include the arginine-rich region of HIV-1 Tat as set forth in Figure 1A. This single molecule displayed a high binding affinity for HIV-1 TAR RNA. Applicants may wish to amend the claim language to clearly set forth the chemical structure of the compound. The disclosure fails to provide adequate support for any other compounds and fails to provide any meaningful data pertaining to the *in vivo* and ex *vivo* activities of the compounds.

The legal considerations that govern enablement determinations pertaining to undue experimentation have been clearly set forth. Enzo Biochem, Inc., 52 U.S.P.Q.2d 1129 (C.A.F.C. 1999). In re Wands, 8 U.S.P.Q.2d 1400 (C.A.F.C. 1988). Ex parte Forman 230 U.S.P.Q. 546 (PTO Bd. Pat. App. Int., 1986). The courts concluded that several factual inquiries should be considered when making such assessments including the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the

invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims. *In re Rainer*, 52 C.C.P.A. 1593, 347 F.2d 574, 146 U.S.P.Q. 218 (1965). The disclosure fails to provide adequate guidance pertaining to a number of these considerations as follows:

- 1) The claims encompass a large genus of compounds that are poorly described in the specification. The only structural requirements set forth in the claim language are that the compound comprise an oligourea of undefined structure and that it comprise a basic-arginine-rich region. The disclosure fails to provide sufficient guidance pertaining to the chemical structure of the claimed oligourea and acceptable side-chain substitutions.
- 2) The disclosure fails to provide sufficient guidance pertaining to the pharmacological profile of any of the Tat-derived oligourea derivatives. HIV antivirals have suffered from a number of welldocumented problems including drug sequestration by serum proteins, half-lives, rapid clearance rates, serum target sufficient and the inability to bioavailabilities, quantities of the drug to desired sites, drug resistance due to the quasispecies nature of HIV-1 infection, and the uneven distribution of the compound throughout the body (Gait and Karn, 1995). The disclosure fails to provide any guidance pertaining to any of these factors.
- 3) The prior art teaches that the generation of successful HIV-1 antivirals is a difficult, complex, and often unpredictable process. Several factors have contributed to antiviral failure including short serum half-lives, poor bioavailabilities, rapid clearance rates, sequestration of the drug by serum proteins, drug resistance due to the quasispecies nature of HIV-1 infection, and the uneven distribution of the compound throughout the body (Gait and Karn, 1995). The disclosure fails to address any of these concerns.

4) The disclosure fails to provide any in vivo or clinical working embodiments. The only data provided in the disclosure demonstrated that a single oligourea derivative was capable of binding to the HIV-1 Tar region with high affinity. However, the disclosure failed to provide any meaningful data from a relevant animal model or preliminary clinical data demonstrating that the claimed compound could cause meaningful deductions in the viral load. HIV-infected patients produce  $10^8-10^{10}$  virions per day. In order for any putative antiviral to produce meaningful clinical results it must be capable of reducing the viral burden considerably. Moreover, the compound must be capable of being targeted to appropriate tissues (i.e., lymphatic compartment) in sufficient quantities to inhibit viral fails to provide any replication. The disclosure all issues. Accordingly, when pertaining to these aforementioned factors are considered in toto, it would clearly require undue experimentation from the skilled artisan to practice the claimed invention.

### Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, James C. Housel, can be reached at (571) 272-0902. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Formal communications may be submitted through the official facsimile number which is (703) 872-9306. Hand-carried formal communications should be directed toward the customer window located in Crystal Plaza Two, 2011 South Clark Place, Arlington, VA. Applicants are directed toward the O.G. Notice for further guidance. 1280 O.G. 681. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

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http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

Jeffrey S. Parkin, Ph.D. Primary Examiner

Art Unit 1648

12 November, 2004